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# Acupuncture in Patients Suffering from Allergic Asthma: Is It Worth Additional Costs?

Thomas Reinhold, PhD, Benno Brinkhaus, MD, Stefan N. Willich, MD, and Claudia Witt, MD

## Abstract

**Objectives:** Acupuncture is increasingly used in patients with allergic asthma, but there is a lack of evidence on the cost–benefit relationship of this treatment. The aim of this study was to assess economic aspects of additional acupuncture treatment in patients with allergic bronchial asthma compared to patients receiving routine care alone.

**Design, subjects, intervention, outcome measures:** In a randomized controlled trial, patients with allergic bronchial asthma were either allocated to a group receiving acupuncture immediately or a waiting-list control group. Both groups were free to use routine care treatment. The resource consumption, costs, and health-related quality of life were evaluated at baseline, and after 3 and 6 months by using statutory health insurance information and standardized questionnaires. Main economic outcome parameters were direct and indirect cost differences during the study period and the incremental cost-effectiveness ratio (ICER) of acupuncture treatment.

**Results:** Three hundred and six (306) patients (159 acupuncture; 147 controls) were included (mean age  $46.5 \pm 13.11$  years, female 57.2%) and were comparable at baseline. Acupuncture treatment was associated with significantly higher costs compared to control patients (overall costs: €860.76 [95% confidence interval (CI) 705.04–1016.47] versus €518.80 [95% CI 356.66–680.93];  $p = 0.003$ ; asthma-related costs: €517.52 [95% CI 485.63–549.40] versus €144.87 [95% CI 111.70–178.05];  $p < 0.001$ ). These additional costs seem essentially driven by acupuncture costs themselves (€378.40 [95% CI 367.10–389.69]). However, acupuncture was associated with superior effectiveness in terms of quality-adjusted life years (QALYs). Resulting ICER lay between €23,231 (overall) and €25,315 (diagnosis-specific) per additional QALY. When using German acupuncture prices of year 2012, the ICER would improve to €12,810 (overall) versus €14,911 (diagnosis-specific) per QALY gained.

**Conclusions:** Treating patients who have allergic bronchial asthma with acupuncture in addition to routine care resulted in additional costs and better effects in terms of patients' quality of life. Acupuncture therefore seems to be a useful and cost-effective add-on treatment.

## Introduction

ASTHMA IS ONE OF THE most common chronic disorders in developed countries.<sup>1</sup> The prevalence varies from country to country and has been estimated to be 7% in France and Germany up to 11% in the United States and 15%–18% in the United Kingdom.<sup>2</sup> Worldwide the literature indicates that about 300 million people are suffering from this disorder.<sup>3</sup>

Often asthma is not well controlled and is associated with additional restrictions in daily life as well as the resulting quality of life.<sup>3,4</sup> The disease starts in childhood and is highly prevalent up to old age. The current studies indicate that most asthma cases are due to allergic conditions. Studies indicate that 90% of all asthma patients had symptoms cor-

related with allergic rhinitis and 38% of rhinitis patients also had asthmatic symptoms.<sup>5</sup>

Beside this, asthma is associated with a remarkable economic burden, while hospitalization and medications were found to be the most important cost drivers of direct costs; the indirect costs were mainly driven by work and school loss.<sup>6</sup> In Germany, the annual patient-related direct and indirect costs range between €2202 for children and €7745 for adults with moderate asthma, and between €7928 and €9,286, respectively, for children and adults with severe asthma (year 2000).<sup>7</sup> In 2008, the Federal Statistical Office calculated total direct costs of about €1.8 billion for Germany.<sup>8</sup> Assuming that the proportion of indirect costs on total amount of disease burden is given as 45%,<sup>9</sup> the total asthma costs in 2008 can be estimated to be €3.3 billion.

Despite advances in pharmacotherapy, complementary and alternative medicine is widely used by patients suffering from allergic disorders. A German study found that about 26.5% of patients received such therapies because of their allergy.<sup>10</sup> This fact supports the economic evaluation of nonpharmacological treatment options, such as acupuncture. In Germany, acupuncture is mainly administered by physicians. The treatment is a relatively resource-intensive intervention due to the time involved for physicians and patients alike.<sup>11</sup> To date, there is a lack of information on costs and cost-benefit relationship of acupuncture compared to routine-care treatment.

## Objective

The main objective of the present health-economic analysis was to compare effectiveness and costs of an additional acupuncture treatment in patients with bronchial asthma compared to routine care alone.

## Methods

### *Study design and patients*

In this pragmatic<sup>12</sup> multicenter, randomized, controlled trial, patients ( $\geq 18$  years of age) with a clinical diagnosis of allergic bronchial asthma (ICD-codes: J44.8, J44.9, J45.0; J45.1, J45.8, J45.9, J46) were enrolled after contacting the participating physician until 2001. Allergic asthma was defined as an inflammatory disease of the airways with bronchial hyperactivity and variable airway obstruction, often associated with an atopic predisposition. Other respiratory diseases or expiratory dyspnea, as well as the suspicion of bronchial asthma with nonallergic origin, were exclusion criteria.

The diagnosis of asthma was conducted as always done in the health insurance system, and the tests used have been documented by the participating doctors. After giving their informed consent, patients were randomly allocated to an acupuncture group that received immediate acupuncture treatment over a period of 3 months after study or to a waiting-list control group that received delayed acupuncture treatment between months 3 to 6. Patients in both groups were free to use conventional routine medical care as usually compensated by the German statutory health insurance companies.

Participating physicians were required to have received at least 140 hours of acupuncture training. The number, length, and diameter of the needles and the selection of acupuncture points were decided on by the participating doctors themselves and for each patient individually. The acupuncture treatments consisted of 10–15 acupuncture sessions during the study period.

The study project was approved by the Ethics committee of Charité–University Medical Center Berlin/Germany (No. 1424/2000). Further detailed information on the study project (trial registration number DRKS00003767) were already published elsewhere.<sup>13</sup>

### *Resource consumption and cost measurement*

The costs were determined bottom-up, by monetary valuation of a patient's resource consumption during the period of 3 months after randomization. Information on the resource use was obtained by using statutory health insurance

databases provided by "Techniker Krankenkasse" (Technicians' Health Insurance Comp.). Costs considered were direct health care such as costs physicians' visits, hospital stays (without consideration of private individual billing) as well as prescription drugs (including patient's co-payment) and the costs of acupuncture sessions itself. In our study, €35 were paid for each acupuncture session (base-case). To also reflect the current cost-effectiveness of acupuncture, 2012 acupuncture prices of €21 per session were used in a sensitivity analysis.

The cost perspective of the study was societal. Therefore, in addition to health insurance costs we also considered indirect costs caused by patients' work incapacity. These indirect costs were determined by using the human capital approach<sup>14</sup> and were estimated to be about €78 per day sick away from work.

During the first 3 months of direct comparison, the following were calculated: (1) diagnosis-specific costs using ICD-10 codes to identify costs due to only allergic bronchial asthma and related conditions and (2) the overall costs after randomization, including costs not related to allergic asthma.

### *Outcome measurement and quality-adjusted life year determination*

Effectiveness was evaluated using quality-of-life data determined with the 36-Item Short Form Health Survey (SF-36).<sup>15</sup> This questionnaire consists of 36 questions, is self-administered, and assesses quality of life and well-being in 8 subscales regarding physical functioning and perception of physical role, vitality, general and mental health, perception of emotional role, social functioning, and bodily pain. Patients were asked to complete this questionnaire at baseline, and after 3 months and 6 months. These SF-36 quality-of-life-data were converted to health-state utilities using an algorithm developed by Brazier et al.<sup>16</sup> As a result, such health-state utilities were obtained for the time points: baseline, 3 months, as well as 6 months after study onset. Between these time points, the common assumption of a linear change of health-state utilities over time was used.<sup>17</sup>

Since the control group did also receive acupuncture after their waiting time of 3 months, it was not possible to perform a direct group comparison during months 3 and 6. Otherwise, if the comparison would only be restricted to the first 3 months of the study, it would not be disclosed that acupuncture patients might experience further acupuncture effects on their quality of life. In order to achieve a longer comparison period, it was assumed that control patients would not get acupuncture between months 3 and 6. Therefore, a further assumption was that the utility-trend in control patients during the time would be the same as was observed in the acupuncture patients. Based on this, a new utility for time point 6 months after baseline was modeled for control patients. The utilities in acupuncture were taken as reported. After that, the resulting quality-adjusted life years (QALYs) were calculated by adopting the area-under-the-curve method.<sup>17,18</sup>

### *Cost-effectiveness assessment*

Cost-effectiveness analysis was calculated for all randomized patients with complete data on costs and effects. Since the intervention effects were considered in terms of

quality of life, the cost-effectiveness measurement was performed as a cost-utility analysis. In case of superior quality of life compared to control patients, the cost-effectiveness of acupuncture was calculated as the relation between group differences in costs and differences in QALYs, the so-called incremental cost-effectiveness ratio (ICER):

$$\text{ICER} = \frac{\text{mean costs}_{\text{acupuncture}} - \text{mean costs}_{\text{controls}}}{\text{mean QALYs}_{\text{acupuncture}} - \text{mean QALYs}_{\text{controls}}}$$

The ICER reflects the additional costs associated with realizing 1 additional QALY compared to the control patients. In health economic studies, particularly in Western Europe, a threshold  $\lambda$  up to €50,000 per QALY gained is often used to decide whether an intervention is cost-effective or not.<sup>19</sup> A health technology can be seen as a cost-effective intervention (in terms of value for money), if the realization of one additional QALY is reachable with less than €50,000. Thus, the threshold  $\lambda$  is often described as society's willingness to pay for 1 extra QALY. This threshold was also used in order to reach a better comparability of international study results, knowing well that such a threshold does not yet exist in German health care decision-making.

Additionally, the net benefit approach<sup>20</sup> was used to measure the incremental cost-effectiveness against different societal threshold values  $\lambda$ . For a given threshold value  $\lambda$ , an intervention would be considered to be cost-effective if its net benefit is greater than zero.<sup>21</sup> The net benefit is defined by the following relation:

$$\text{Net benefit} = (\lambda * \text{QALYs}_{\text{gained for acupuncture}}) - (\text{mean costs}_{\text{acupuncture}} - \text{mean costs}_{\text{control}})$$

To derive cost-effectiveness acceptability curves, nonparametric bootstrapping was used.<sup>22</sup> When using the bootstrap approach, repeated random samples of the same size as the original population are drawn with replacement from the data. In this study's analysis, the original sample was bootstrapped 1000 times to obtain 1000 means for cost and effect differences and the resulting ICERs. These bootstrapped results were transformed into net benefit values under varying threshold values and then plotted in a cost-effectiveness acceptability curve. The cost-effectiveness acceptability curve shows the probability that an intervention is cost-effective against different values of  $\lambda$ .<sup>21</sup> For example: For each of the 1000 bootstrapped cost- and effect-differences, the net benefit was calculated against assumed values, reflecting society's willingness to pay for an additional QALY (e.g.,  $\lambda = €20,000$ ). In the case that 250 of the resulting 1000 net-benefit results were larger than zero, it was concluded that the probability of cost-effectiveness was 25%. Additionally, the bootstrap samples were used to get a graphical overview on the distribution of incremental cost-effectiveness ratios.

### Statistical analyses

Socioeconomic data at baseline were analyzed by using Student's *t*-test for comparing continuous variables (e.g., patient's age, disease duration) and  $\chi^2$  test for dichotomous variables (e.g., gender). Baseline costs in both groups were analyzed using Mann-Whitney *U* test. Furthermore, analysis

of covariance was applied for estimation and comparison of adjusted cost and effectiveness values for months 3 and 6. Adjusting variables were age, gender, education, duration of disease, number of comorbidities, AQLQ-Score (Asthma Quality of Life Questionnaire) at baseline, health-state utility at baseline and the respective baseline value. To derive cost-effectiveness acceptability curves, nonparametric bootstrapping were used, as described above.

The significance level was 5% (two-sided). For inferential statistics, we used SPSS<sup>®</sup> version 11.0. Finally, we used MS Excel<sup>®</sup> 2003 to model bootstrapped cost-effectiveness analyses.

## Results

### Baseline characteristics

A total of 357 patients suffering from allergic asthma were randomized after initial contact with the participating physicians. Three hundred and six (306) of them (159 acupuncture; 147 controls) with complete dataset could be analyzed within the economic analyses (Fig. 1). Participating patients had a mean age of  $46.5 \pm 13.11$  years and were mostly female (57.2%). With regard to socioeconomic variables at baseline, there were no relevant group-differences detectable and also patient's quality of life, reflected by AQLQ-Score (restricted to asthma-related quality of life) as well as Health-state utilities, seems comparable in both groups (Table 1).

### Resource consumption and costs

The patient groups were comparable in terms of their resource consumption prior to the study, with the exception of asthma-related outpatient contacts. As documented in Table 1, patients allocated to the acupuncture group experienced more physician visits than patients of the control group ( $1.63 \pm 5.59$  visits versus  $0.82 \pm 3.17$  visits;  $p=0.040$ ). This difference is also reflected in outpatient costs related to asthma ( $23.01 \pm 87.53$  Euro versus  $11.47 \pm 44.82$  Euro;  $p=0.041$ ). Compared to controls, the total overall costs of patients assigned to the acupuncture group were found to be slightly higher at baseline ( $€636.01 \pm €1180.52$  Euro versus  $€526.92 \pm €1341.08$  Euro;  $p=0.035$ ).

During the study, the acupuncture patients received a mean number of 10.8 (95% CI 10.4–11.3) acupuncture sessions (Table 2). However, this additional intervention did not lead to a substantial reduction of consumed resources and following costs in other health care areas. The mean overall costs of acupuncture patients during the study period were significant higher than for controls (overall:  $€860.76$ ; 95% CI  $€705.04$ – $€1016.47$ ) versus  $€518.80$  (95% CI  $€356.66$ – $€680.93$ );  $p=0.003$ , asthma-related:  $€517.52$  (95% CI  $€485.63$ – $€549.40$ ) versus  $€144.87$  (95% CI  $€111.70$ – $€178.05$ );  $p<0.001$ ). The mean cost difference between both treatment groups (overall:  $€341.96$ ; 95% CI  $€115.88$ – $€568.04$ ; asthma-related:  $€372.65$ ; 95% CI  $€326.36$ – $€418.93$ ) seems essentially driven by the acupuncture costs itself ( $€378.40$ ; 95% CI  $€367.10$ – $€389.69$ ). After excluding acupuncture session costs we found no longer a significant difference in costs between both treatment arms (overall:  $€477.17$ ; 95% CI  $€321.35$ – $€633.00$ ) versus  $€518.80$ ; 95% CI  $€356.66$ – $€680.93$ ;  $p=0.718$

FIG. 1. Study flowchart.

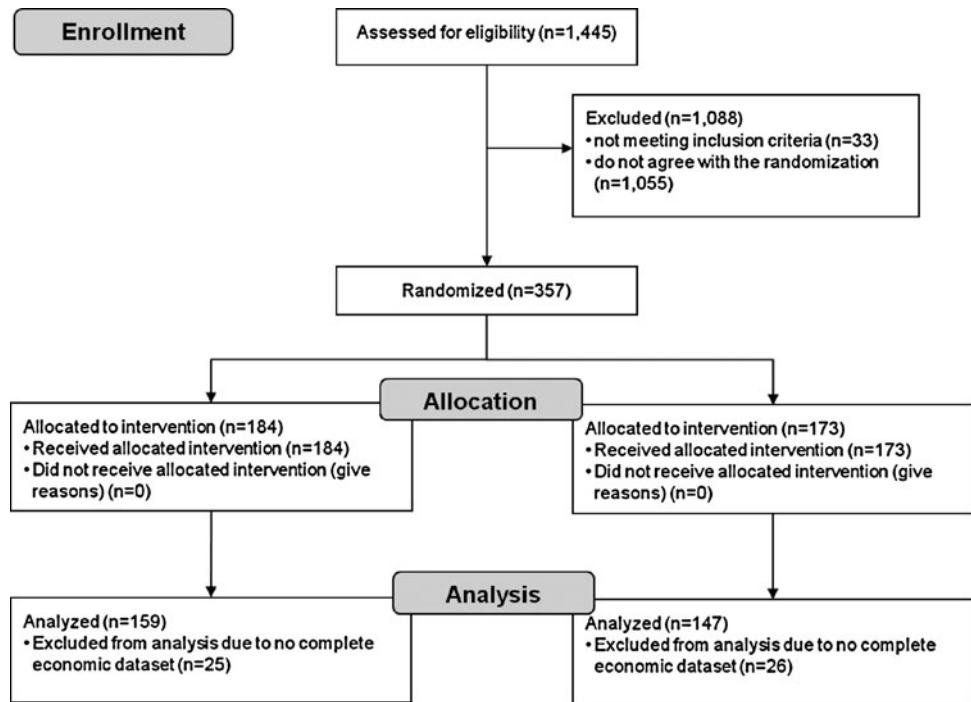


TABLE 1. BASELINE PATIENT'S CHARACTERISTICS, RESOURCE CONSUMPTION AND COSTS DURING 3 MONTHS BEFORE STUDY ONSET

	Acupuncture (n=159)	Control (n=147)	p-Value
Sociodemographic characteristics (in % [n] resp. mean $\pm$ SD)			
Proportion of female patients	59.1% (94)	55.1% (81)	0.490
Patients age (years)	46.78 $\pm$ 12.41	46.31 $\pm$ 13.86	0.751
Patients > 10 years of school	44.0% (70)	49.0% (72)	0.423
Disease duration (years)	14.32 $\pm$ 12.84	12.6 $\pm$ 11.64	0.229
Mean number of comorbidities	0.59 $\pm$ 1.08	0.54 $\pm$ 0.97	0.646
AQLQ score	4.37 $\pm$ 1.12	4.47 $\pm$ 0.93	0.425
Health-state utility	0.6979 $\pm$ 0.1239	0.7191 $\pm$ 0.1107	0.116
Asthma-related quantity of resource consumption (mean number $\pm$ SD)			
Outpatient visits	1.63 $\pm$ 5.59	0.82 $\pm$ 3.17	0.040
Drug-prescriptions	2.03 $\pm$ 2.47	1.84 $\pm$ 2.32	0.740
Hospital days	0.06 $\pm$ 0.79	—	0.336
Days of work incapacity	0.30 $\pm$ 1.60	0.14 $\pm$ 1.29	0.190
Asthma-related costs in euros (mean costs per patient $\pm$ SD)			
Outpatient visits	23.01 $\pm$ 87.53	11.47 $\pm$ 44.82	0.041
Medication	89.97 $\pm$ 123.19	87.00 $\pm$ 148.00	0.715
Hospital stays	11.71 $\pm$ 147.66	—	0.336
Indirect costs	23.59 $\pm$ 125.17	20.20 $\pm$ 163.09	0.378
Total asthma-related costs	148.29 $\pm$ 264.94	118.66 $\pm$ 231.57	0.096
Overall quantity of resource consumption (mean number $\pm$ SD)			
Outpatient visits	2.40 $\pm$ 5.82	2.04 $\pm$ 4.53	0.306
Drug prescriptions	5.38 $\pm$ 5.51	4.31 $\pm$ 4.62	0.132
Hospital days	0.67 $\pm$ 2.80	0.30 $\pm$ 1.90	0.077
Days of work incapacity	2.76 $\pm$ 7.69	1.81 $\pm$ 5.08	0.078
Overall costs in euros (mean costs per patient $\pm$ SD)			
Outpatient visits	33.37 $\pm$ 90.01	27.72 $\pm$ 61.97	0.318
Medication	178.65 $\pm$ 272.27	155.97 $\pm$ 286.60	0.242
Hospital stays	198.14 $\pm$ 875.27	88.25 $\pm$ 595.18	0.077
Indirect costs	225.85 $\pm$ 697.31	254.98 $\pm$ 961.01	0.124
Total overall costs	636.01 $\pm$ 1180.52	526.92 $\pm$ 1341.08	0.035

AQLQ, Asthma Quality of Life Questionnaire; resp., respectively.



TABLE 2. OUTCOMES, RESOURCE CONSUMPTION AND COSTS DURING THE STUDY PERIOD

	Acupuncture (n=159)	Control (n=147)	p-Value
Outcomes used for cost-effectiveness analyses (mean [95% CI]) <sup>a</sup>			
Health-state utility 3 months	0.7623 (0.7468–0.7778)	0.7172 (0.7011–0.7334)	<0.001
Health-state utility 6 months	0.7754 (0.7591–0.7918)	0.7320 (0.7156–0.7485)	<0.001
QALYs	0.3754 (0.3696–0.3812)	0.3592 (0.3534–0.3650)	<0.001
Asthma-related quantity of resource consumption (mean number [95% CI]) <sup>a</sup>			
Acupuncture sessions	10.81 (10.49–11.13)	—	<0.001
Outpatient visits	2.02 (1.16–2.88)	2.16 (1.27–3.06)	0.817
Drug-prescriptions	2.19 (1.89–2.49)	2.04 (1.73–2.35)	0.490
Hospital days	—	—	—
Days of work incapacity	0.09 (0.02–0.17)	0.02 (0.00–0.10)	0.195
Asthma-related costs in euros (mean costs per patient [95% CI]) <sup>a</sup>			
Acupuncture	378.40 (367.10–389.69)	—	<0.001
Outpatient visits	27.80 (15.29–40.32)	30.03 (17.02–43.05)	0.809
Medication	102.73 (85.53–119.92)	94.10 (76.21–112.00)	0.497
Hospital stays	—	—	—
Indirect costs	5.56 (0.00–20.38)	18.21 (2.78–33.63)	0.248
Total asthma related costs	517.52 (485.63–549.40)	144.87 (111.70–178.05)	<0.001
Total asthma-related costs minus costs of acupuncture	134.22 (105.31–163.13)	144.87 (111.70–178.05)	0.631
Overall quantity of resource consumption (mean number [95% CI]) <sup>a</sup>			
Acupuncture sessions	10.81 (10.49–11.13)	—	<0.001
Outpatient visits	3.57 (2.47–4.66)	4.90 (3.76–6.04)	0.100
Drug-prescriptions	5.36 (4.73–6.00)	5.33 (4.67–6.00)	0.944
Hospital days	0.28 (0.00–0.60)	0.35 (0.02–0.68)	0.763
Days of work incapacity	1.32 (0.56–2.09)	1.24 (0.45–2.04)	0.886
Overall costs in euros (mean costs per patient [95% CI]) <sup>a</sup>			
Acupuncture	378.40 (367.10–389.69)	—	<0.001
Outpatient visits	49.29 (33.50–65.08)	67.32 (50.89–83.75)	0.122
Medication	186.69 (157.32–216.06)	166.26 (135.69–196.83)	0.346
Hospital stays	85.26 (0.00–191.389)	104.94 (0.00–215.43)	0.802
Indirect costs	161.07 (80.20–241.94)	179.31 (95.16–263.45)	0.760
Total overall costs	860.76 (705.04–1,016.47)	518.80 (356.66–680.93)	0.003
Total overall costs minus costs of acupuncture	477.17 (321.35–633.00)	518.80 (356.66–680.93)	0.718

<sup>a</sup> Adjusted for: age, gender, education, duration of disease, number of comorbidities, AQLQ score at baseline, health-state utility at baseline, respective baseline value.

CI, confidence interval; QALY, quality-adjusted life year.

(asthma-related: €134.22; 95% CI €105.31–€163.13) versus €144.87 (95% CI €111.70–€178.05);  $p=0.631$ ).

### Effectiveness

During the first 3 months of the study, the patients receiving acupuncture experienced a considerable improvement (Fig. 2). The mean health state utilities increased from 0.6979 (95% CI 0.6786–0.7173) at baseline to 0.7623 (95% CI 0.7468–0.7778) 3 months after. However, although no further acupuncture sessions were offered to these patients after the first 3 months of the study, further improvements in quality of life were observed between months 3 and 6. The utility 6 months after study onset increased to 0.7754 (95% CI 0.7591–0.7918). In contrast, patients allocated to the control group showed no changes in their quality of life assessment during the first 3 months of the study. Between months 3 and 6, these patients were also able to receive acupuncture. As a result, a comparable quality-of-life improvement as observed in acupuncture patients during the first 3 months was detectable.

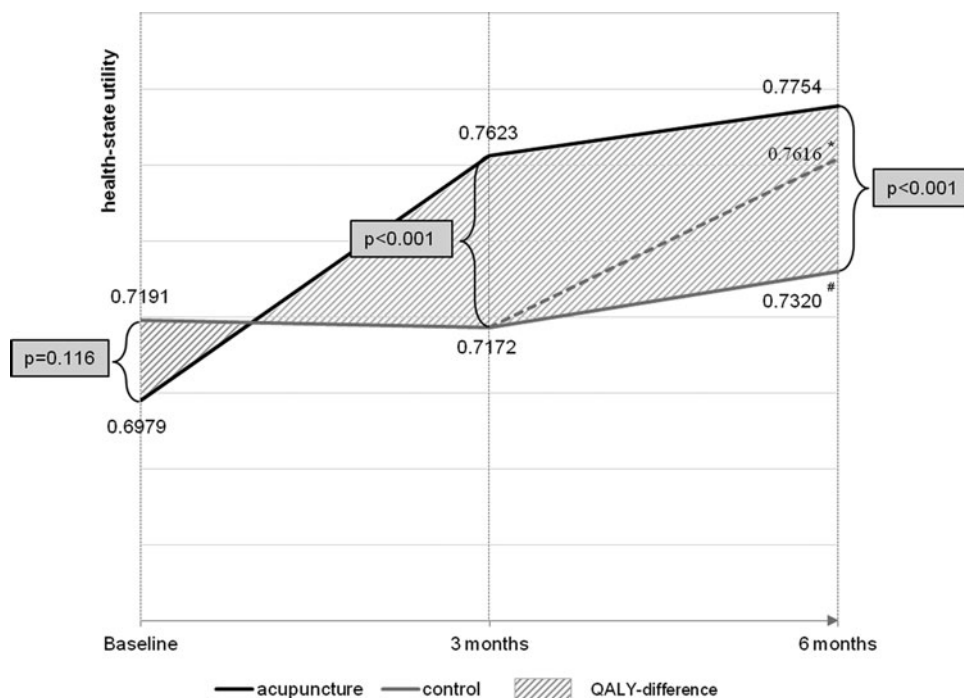
According to the previous assumption that control patients would not get acupuncture between months 3 and 6, the resulting QALYs for that group were 0.3592 (95% CI

0.3534–0.3650). That is significant less ( $p<0.001$ ) compared to acupuncture patients who experienced mean QALYs of 0.3754 (95% CI 0.3696–0.3812).

### Cost-effectiveness assessment

Economic analysis has shown higher costs in the acupuncture group compared to the control group. On the other hand, acupuncture is more effective. This result has proven to be robust in bootstrap analyses (Fig. 3; the majority of 1000 bootstrapped results are located in the upper right-hand quadrant). The mean ICER was calculated as relation of cost- and effect-differences between both groups (Table 3) and was found to be €23,231 per QALY gained (including overall costs) and €25,315 per additional QALY (including only asthma-related costs). According to the most threshold value of €50,000 per QALY gained, acupuncture must be considered as a cost-effective treatment in patients suffering from allergic asthma with a probability between 86.5% and 88.5% (Fig. 4). Assuming that society's willingness to pay would be lower than the assumed €50,000, the probability of cost-effectiveness will also decrease.

**FIG. 2.** Course of health-state utilities during the study. \*Real health-state utility of control patients; #modeled new health-state utility of control patients (assumption: did not receive acupuncture during months 3 and 6). QALY, quality-adjusted life year.



**FIG. 3.** Bootstrapped results on differences in costs and effects between the treatment groups.

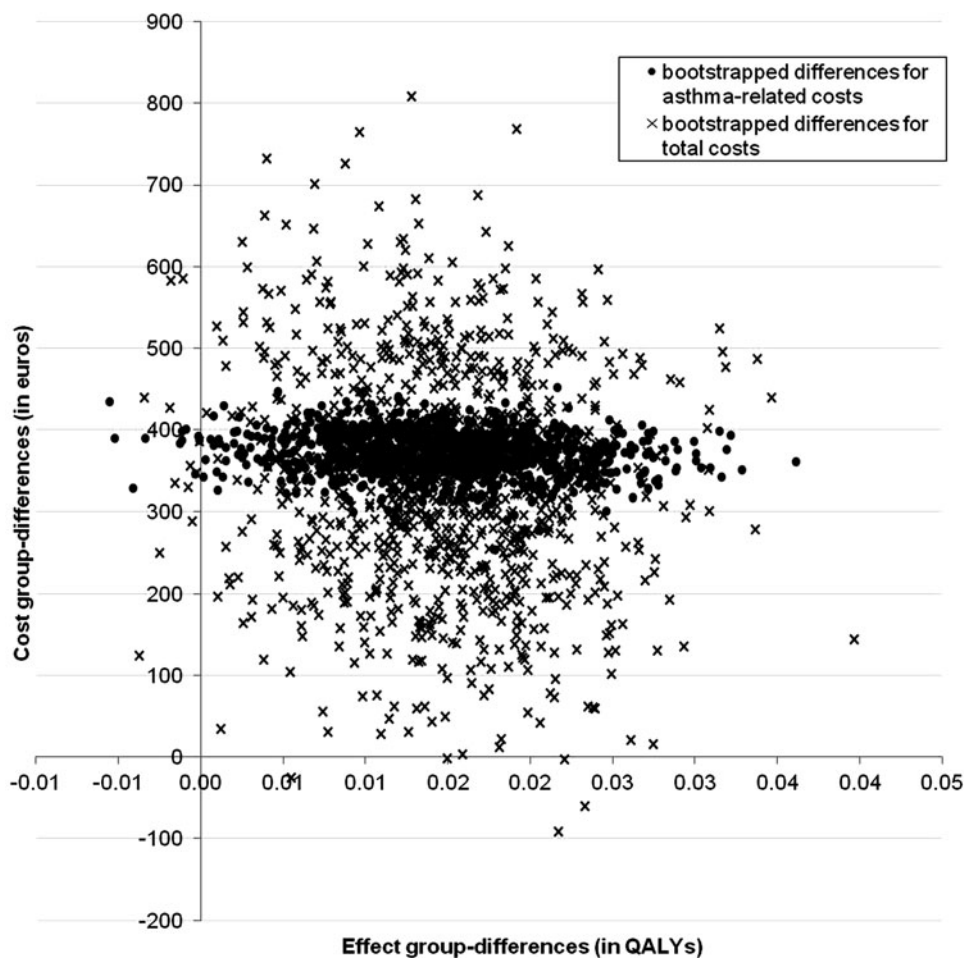


TABLE 3. INCREMENTAL COST-EFFECTIVENESS RESULTS

Group differences (mean [95% CI]) <sup>a</sup>		p-Value
QALYs	0.0147 (0.0061–0.0234)	0.001
Asthma-related cost (in euros)	372.64 (326.36–418.93)	<0.001
Overall costs (in euros)	341.96 (115.88–568.04)	0.003
Resulting ICER in euros (base case)		
For asthma-related costs		
Mean	25,315	
Median (IQR) <sup>b</sup>	24,822 (15,664)	
For overall costs		
Mean	23,231	
Median (IQR) <sup>b</sup>	23,163 (20,276)	
ICER in euros based on 2012 acupuncture prices		
For asthma-related costs		
Mean	14,911	
Median (IQR) <sup>b</sup>	14,513 (10,337)	
For total costs		
Mean	12,810	
Median (IQR) <sup>b</sup>	12,750 (15,822)	

<sup>a</sup>Adjusted for: age, gender, education, duration of disease, number of comorbidities, AQLQ score at baseline, health-state utility at baseline, respective baseline value.

<sup>b</sup>Median (IQR) were obtained based on bootstrapped ICER results. ICER, incremental cost-effectiveness ratio; IQR, interquartile range.

As a result of decreasing reimbursement rates for acupuncture sessions during the last years in Germany, the ICER was additionally calculated using 2012 acupuncture prices of €21 per session (base case: €35 per session). The mean ICER would decrease to €12,810 (including overall costs) and €14,911 (including asthma-related costs)

for realizing one additional QALY, showing an increased cost-effectiveness. Assuming a threshold value of €50,000, the probability of cost-effectiveness would improve to values ranging from 91.4% to 94.2%.

## Discussion

Acupuncture in addition to routine care compared with routine care alone was associated with better quality of life as well as higher costs. This increase of costs was essentially due to acupuncture costs and was not compensated for by relevant savings in other health care components during the study period. The ICER lay between €23,231 (overall) and €25,315 (diagnosis-specific) per QALY gained. When adopting a threshold of €50,000 per additional QALY, acupuncture in addition to routine care is cost-effective.

The present study includes, to the authors' knowledge, the first calculation of cost-effectiveness for acupuncture treatment in patients with allergic bronchial asthma. The underlying large sample size allows a robust estimation of costs and effects and is an important basis for a comprehensive economic assessment. A further strength is the randomized setting embedded in regular health care that allows drawing conclusions from the study to everyday treatment.

Nevertheless, some potential limitations should be kept in mind when interpreting the results of this investigation. A first limitation results from the fact that the only source of information for resource consumption and costs consisted of the statutory health insurance companies' databases. Thus, private expenses such as over-the-counter medication or add-on therapies not reimbursed by the statutory health insurance system could not be included.

Another discussion point arises from the design and duration of the study. The cost and effectiveness data were directly comparable between the two groups for the duration of 3 months after baseline, since subsequently patients in the

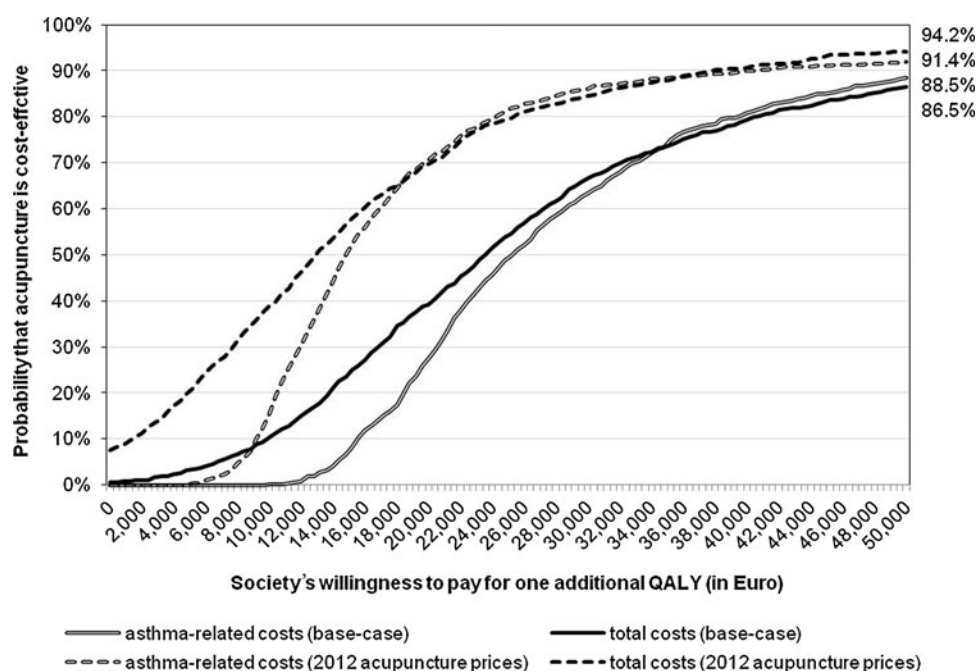


FIG. 4. Cost-effectiveness probability of additional acupuncture along different values of society's willingness to pay.



waiting-list control group were also offered acupuncture. However, although no further acupuncture sessions were offered to the acupuncture patients after the first 3 months of the study, further improvements were observed in quality of life between months 3 and 6. Comparing both groups only over the first 3 months would lead to an unjustified underestimation of acupuncture effects. As is stated in the Methods section, we decided to extend the comparison over the complete period of 6 months. Therefore, it was assumed that control patients would not get acupuncture between months 3 and 6 and that subsequently they would not have experienced an acupuncture-driven improvement in their quality of life as was observed in reality. However, the problem arises that it was unknown what proportion of the observed improvement in quality of life was achieved by acupuncture itself, and what proportion might have been a consequence of seasonal effects (e.g., reduction in allergic symptoms severity due to a seasonal reduced pollen concentration). To handle this difficulty, it was assumed that control patients would experience at least the same quality-of-life improvement as that observed in the acupuncture group between months 3 and 6. This assumption is reflected by a new modeled 6-month utility for control patients, implying that the utility trend in control patients during the time would be the same as was observed in the acupuncture patients (see the Methods section, and Fig. 2).

Furthermore, the study gives a good example for changes in cost-effectiveness appraisal over the time. The base-case analyses presented in the study used a reimbursement rate of €35 per single acupuncture session. It is important to know that for services regularly reimbursed by statutory health insurance companies, no market prices exist in Germany. Reimbursement rates are rather administratively fixed fees (not necessarily related to the real costs induced by the use of general practitioners for the procedure) resulting from negotiations between the German general practitioners' organizations and the statutory health insurance companies. In this fee, costs for needles and other consumables are supposed to be included. For taking into account recent trends in reimbursement rates, the cost-effectiveness results were updated by conducting a sensitivity analysis with 2012 acupuncture costs of €21. Expectedly, the cost-effectiveness of acupuncture will increase, but such an isolated view on financial aspects can also lead to another interpretation. One might speculate, however, that a reduction in physicians' payment could perhaps result in lower treatment effects, maybe due to less motivated doctors or reduced time invested for conducting the acupuncture.

The main result of the present study is in range with a number of trials investigating the cost-effectiveness of acupuncture for different indications. For example, acupuncture was found to be a cost-effective treatment in patients suffering from musculoskeletal disorders such as low back pain, neck pain, or in patients suffering from osteoarthritis.<sup>23–25</sup> With regard to allergic disorders, acupuncture was, and is still investigated in patients with allergic rhinitis so far<sup>26</sup> and was also found to be cost-effective in one large German study (ICER €17,377 per QALY gained).<sup>27</sup> Keeping in mind the possible link between allergic rhinitis and the development of allergic asthma,<sup>28,29</sup> acupuncture may offer an additional therapeutic option for reducing allergic symptoms and improving patients' well-being.

## Conclusions

In conclusion, this study shows that treating patients who have allergic bronchial asthma with acupuncture in addition to routine care resulted in additional costs and better effects in terms of patients' quality of life. Acupuncture therefore seems to be a useful and cost-effective add-on treatment.

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## References

- Polosa R, Al-Delaimy WK, Russo C, et al. Greater risk of incident asthma cases in adults with allergic rhinitis and effect of allergen immunotherapy: A retrospective cohort study. *Respir Res* 2005;6:153.
- Peters SP, Ferguson G, Deniz Y, Reisner C. Uncontrolled asthma: A review of the prevalence, disease burden and options for treatment. *Respir Med* 2006;100:1139–1151.
- Demoly P, Paggiaro P, Plaza V, et al. Prevalence of asthma control among adults in France, Germany, Italy, Spain and the UK. *Eur Respir Rev* 2009;18:105–112.
- Briggs AH, Bousquet J, Wallace MV, et al. Cost-effectiveness of asthma control: An economic appraisal of the GOAL study. *Allergy* 2006;61:531–536.
- Corren J. The connection between allergic rhinitis and bronchial asthma. *Curr Opin Pulm Med* 2007;13:13–18.
- Bahadori K, Doyle-Waters MM, Marra C, et al. Economic burden of asthma: A systematic review. *BMC Pulm Med* 2009;9:24.
- Schramm B, Ehlken B, Smala A, et al. Cost of illness of atopic asthma and seasonal allergic rhinitis in Germany: 1-yr retrospective study. *Eur Respir J* 2003;21:116–122.
- The Federal Health Monitoring, Federal Statistical Office Germany (2012) Medical costs in million € for Germany. Online document at: <http://www.gbe-bund.de/> Accessed August 22, 2012.
- The Federal Health Monitoring, Federal Statistical Office Germany (2012) Structure of asthma costs in international comparison. Online document at: <http://www.gbe-bund.de/> Accessed August 22, 2012.
- Schafer T, Riehle A, Wichmann HE, Ring J. Alternative medicine in allergies: Prevalence, patterns of use, and costs. *Allergy* 2002;57:694–700.
- Paterson C, Britten N. Acupuncture as a complex intervention: A holistic model. *J Altern Complement Med* 2004;10:791–801.
- Zwarenstein M, Treweek S, Gagnier JJ, et al. Improving the reporting of pragmatic trials: An extension of the CONSORT statement. *BMJ* 2008;337:a2390.
- Witt C, Brinkhaus B, Jena S, et al. Effectiveness, safety and efficiency of acupuncture: Demonstration Project acupuncture by the Technicians' Health Insurance Company. *Deutsch Arztebl* 2012;103:A187–A195.
- Hanoverian Consensus-Group. German Recommendations for health economic evaluations: Revised version of the

- Hanover Consensus. *Gesundh Ökon Qual Manag* 1999;4: A62–A65.
15. Bullinger M, Kirchberger I. SF-36 Health Survey, Manual. Göttingen: Hogrefe, 1998.
  16. Brazier J, Roberts J, Deverill M. The estimation of a preference-based measure of health from the SF-36. *J Health Econ* 2002;21:271–292.
  17. Richardson G, Manca A. Calculation of quality adjusted life years in the published literature: A review of methodology and transparency. *Health Econ* 2004;13:1203–1210.
  18. Thompson SG, Barber JA. How should cost data in pragmatic randomised trials be analysed? *BMJ* 2000;320:1197–1200.
  19. Greenberg D, Winkelmayr WC, Neumann PJ. Prevailing judgments about society's willingness to pay for QALY or life-year gained. *Int J Public Health* 2005;2(Suppl 1):301.
  20. Zethraeus N, Johannesson M, Jonsson B, et al. Advantages of using the net-benefit approach for analysing uncertainty in economic evaluation studies. *Pharmacoeconomics* 2003;21: 39–48.
  21. Lothgren M, Zethraeus N. Definition, interpretation and calculation of cost-effectiveness acceptability curves. *Health Econ* 2000;9:623–630.
  22. Efron B. Bootstrap methods: Another look at the jackknife. *Ann Statist* 1979;7:1–26.
  23. Witt CM, Jena S, Selim D, et al. Pragmatic randomized trial evaluating the clinical and economic effectiveness of acupuncture for chronic low back pain. *Am J Epidemiol* 2006; 164:487–496.
  24. Reinhold T, Witt CM, Jena S, et al. Quality of life and cost-effectiveness of acupuncture treatment in patients with osteoarthritis pain. *Eur J Health Econ* 2008;9:209–219.
  25. Willich SN, Reinhold T, Selim D, et al. Cost-effectiveness of acupuncture treatment in patients with chronic neck pain. *Pain* 2006;125:107–113.
  26. Witt CM, Brinkhaus B. Efficacy, effectiveness and cost-effectiveness of acupuncture for allergic rhinitis: An overview about previous and ongoing studies. *Auton Neurosci* 2010; 157:42–45.
  27. Witt CM, Reinhold T, Jena S, et al. Cost-effectiveness of acupuncture in women and men with allergic rhinitis: A randomized controlled study in usual care. *Am J Epidemiol* 2009;169:562–571.
  28. Polosa R, Al-Delaimy WK, Russo C, et al. Greater risk of incident asthma cases in adults with allergic rhinitis and effect of allergen immunotherapy: A retrospective cohort study. *Respir Res* 2005;6:153.
  29. Sazonov V, Ambegaonkar BM, Bolge SC, et al. Frequency of diagnosis and treatment of allergic rhinitis among adults with asthma in Germany, France, and the UK: National Health and Wellness Survey. *Curr Med Res Opin* 2009;25: 1721–1726.

Address correspondence to:

Thomas Reinhold, PhD

*Institute for Social Medicine, Epidemiology  
and Health Economics*

*Charité–University Medical Center*

*Luisenstrasse 57, Berlin 10117*

*Germany*

*E-mail: thomas.reinhold@charite.de*